

600-1-179 N

(Sheet 1 of 31)

# E. coli DNA Polymerase III

JC882 U.S. PTO

09/642218

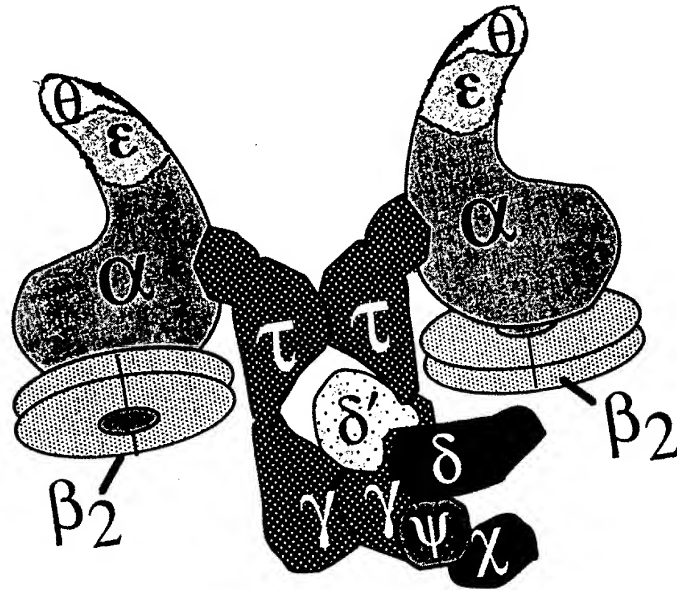


Figure 1

00512218-001000

## ATP binding

E. coli

MSYQVLARKWRPQTFADVVGQEHVLTALANGLSLGRIHHAYLFSGTRGVGKTSIARLLAK

B. subtilis

MSYQALYRVFRPQRFEDVVGQEHITKTLQNALLOKKFSSHAYLFSGPRGTGKTSAAKIFAK

\*\*\*\* \* \* \* \* \* \* \* \* \* \* . \* \* \* . \* \* \* \* \* \* \* \* \* \* \* . \* \*

E. coli

GLNCETGITATPCGVCDNCREIEQGRFVDLIEIDAASRTKVEDTRDLLDNVQYAPARGRF

B. subtilis

AVNCEHAPVDEPCNECAACKGITNGSISDVIEIDAASNNGVDEIRDIRDKVKFAPSAVTY

. \*\*\* . \* \* . \* . \* . \* . \* \* \* \* \* . \* . \* \* . \* \* . \* \* . \* .

E. coli

KVYLIDEVHMLSRHSFNALLKTLEEPPEHVKFLLATTPQKLPVTILSRCLQFHLKALDV

B. subtilis

KVYIIDEVHMLSIGAFNALLKTLEEPPEHCIFILATTEPHKIPLTIISRCQRFDFKRITS

\*\*\* . \*

Figure 2

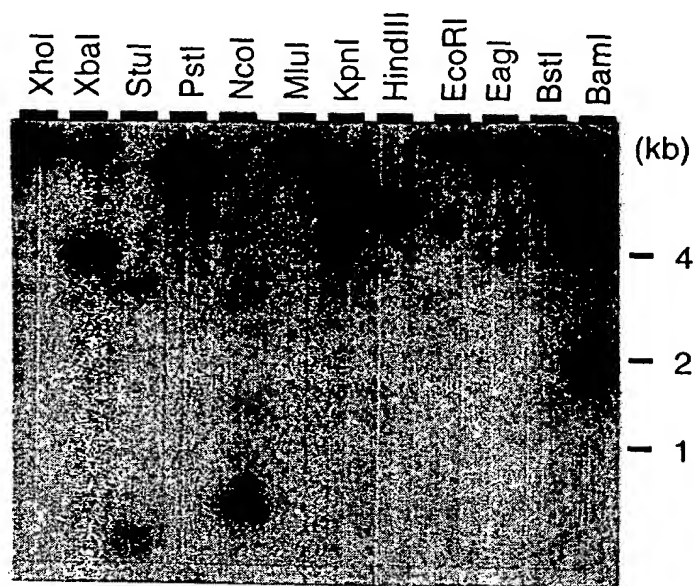


Figure 3

600-1-179 N (Sheet 4 of 31)

TCCGGGGGTG	GGGTTCCCAG	GTAGACCCCG	GCCCCTCCCG	TGAGCCCCTT	TACCCAGGCC	60
GCCACCTCCT	CCAGGGGGGC	CAAGGCGTGC	AAGGAGAGGA	ACGTCCGCAC	<u>CACGCCCTAT</u>	120
					S.D.	
ACTAGCCTT	GTG AGC GCC CTC TAC CGC CGC TTC CGC CCC CTC ACC TTC CAG GAG GTG GTG	met ser ala leu tyr arg arg phe arg pro leu thr phe gln glu val val	180			(17)
					CAC	
GGG CAG GAG CAC GTG AAG GAG CCC CTC CTC AAG GCC ATC CGG GAG GGG AGG CTC GCC CAG	gly gln glu his val lys glu pro leu leu lys ala ile arg glu gly arg leu ala gln	240				(37)
GCS TAC CTS TTC TCC GGS AC						
GCC TAC CTC TTC TCC GGG CCC AGG GGC GTG GGC AAG ACC ACC ACG GCG AGG CTC CTC GCC	ala tyr leu phe ser gly pro arg gly val gly lys thr thr thr ala arg leu leu ala	300				(57)
ATG GCG GTG GGG TGC CAG GGG GAA GAC CCC CCT TGC GGG GTC TGC CCC CAC TGC CAG GCG	met ala val gly cys gln gly glu asp pro pro cys gly val cys pro his cys gln ala	360				(77)
GtG CAG AGG GGC GCC CAC CCG GAC GTG GTG GAC ATT GAC GCC GCC AGC AAC AAC TCC GTG	Val gln arg gly ala his pro asp val val asp ile asp ala ala ser asn asn ser val	420				(97)
GAG GAC GTG CGG GAG CTG AGG GAA AGG ATC CAC CTC GCC CCC CTC TCT GCC CCC AGG AAG	glu asp val arg glu leu arg glu arg ile his leu ala pro leu ser ala pro arg lys	480				(117)
					C	
GTC TTC ATC CTG GAC GAG GCC CAC ATG CTC TCC AAA AGC GCC TTC AAC GCC CTC CTC AAG	Val phe ile leu asp Glu ala his met leu ser lys ser ala phe asn ala leu leu lys	540				(137)
TGS CTS CTC CTC GGS GGS CTC GTG						
ACC CTG GAG GAG CCC CCG CCC CAC GTC CTC TTC GTC TTC GCC ACC ACC GAG CCC GAG AGG	Thr leu glu glu pro pro pro his val leu phe val phe ala thr thr glu pro glu arg	600				(157)
ATG CCC CCC ACC ATC CTC TCC CGC ACC CAG CAC TTC CGC TTC CGC CGC CTC ACG GAG GAG	met pro pro thr ile leu ser arg thr gln his phe arg phe arg arg leu thr glu glu	660				(177)
GAG ATC GCC TTT AAG CTC CGG CGC ATC CTG GAG GCC GTG GGG CGG GAG GCG GAG GAG GAG	glu ile ala phe lys leu arg arg ile leu glu ala val gly arg glu ala glu glu glu	720				(197)
GCC CTC CTC CTC CTC GCC CGC CTG GCG GAC GGG GCC CTT AGG GAC GCG GAA AGC CTC CTG	ala leu leu leu leu ala arg leu ala asp gly ala leu arg asp ala glu ser leu leu	780				(217)
GAG CGC TTC CTC CTC CTG GAA GGC CCC CTC ACC CGG AAG GAG GTG GAG CGC GCC CTA GGC	glu arg phe leu leu leu glu gly pro leu thr arg lys glu val glu arg ala leu gly	840				(237)
TCC CCC CCA GGG ACC GGG GTG GCC GAG ATC GCC GCC TCC CTC GCG AGG GGG AAA ACG GCG	ser pro pro gly thr gly val ala glu ile ala ala ser leu ala arg gly lys thr ala	900				(257)
GAG GCC CTG GGC CTC GCC CGG CGC CTC TAC GGG GAA GGG TAC GCC CCG AGG AGC CTG GTC	glu ala leu gly leu ala arg arg leu tyr gly glu gly tyr ala pro arg ser leu val	960				(277)
TCG GGC CTT TTG GAG GTG TTC CGG GAA GGC CTC TAC GCC GCC TTC GGC CTC GCG GGA ACC	ser gly leu leu glu val phe arg glu gly leu tyr ala ala phe gly leu ala gly thr	1020				(297)
CCC CTT CCC GCC CCG CCC CAG GCC CTG ATC GCC GCC ATG ACC GCC CTG GAC GAG GCC ATG	pro leu pro ala pro pro gln ala leu ile ala ala met thr ala leu asp glu ala met	1080				(317)

Figure 4A

GAG glu	CGC arg	CTC leu	GCC ala	CGC arg	CGC arg	TCC ser	GAC asp	GCC ala	TTA leu	AGC ser	CTG leu	GAG glu	GTG val	GCC ala	CTC leu	CTG leu	GAG glu	GCG ala	GGA gly	1140 (337)		
AGG arg	GCC ala	CTG leu	GCC ala	GCC ala	GAG glu	GCC ala	CTA leu	CCC pro	CAG gln	CCC pro	ACG thr	GGC gly	GCT ala	CCT pro	TCC ser	CCA pro	GAG glu	GTC val	GGC gly	1200 (357)		
CCC pro	AAG lys	CCG pro	GAA glu	AGC ser	CCC pro	CCG pro	ACC thr	CCG pro	GAA glu	CCC pro	CCA pro	AGG arg	CCC pro	GAG glu	GAG glu	GCG ala	CCC pro	GAC asp	CTG leu	1260 (377)		
CGG arg	GAG glu	CGG arg	TGG trp	CGG arg	GCC ala	TTC phe	CTC leu	GAG glu	GCC ala	CTC leu	AGG arg	CCC pro	ACC thr	CTA leu	CGG arg	GCC ala	TTC phe	GTG val	CGG arg	1320 (397)		
GAG glu	GCC ala	CGC arg	CCG pro	GAG glu	GTC val	CGG arg	GAA glu	GGC gly	CAG gln	CTC leu	TGC cys	CTC leu	GCT ala	TTC phe	CCC pro	GAG glu	GAC asp	AAG lys	GCC ala	1380 (417)		
TTC phe	CAC his	TAC tyr	CGC arg	AAG lys	GCC ala	TCG ser	GAA glu	CAG gln	AAG lys	GTG val	AGG arg	CTC leu	CTC leu	CCC pro	CTG leu	GCC ala	CAG gln	GCC ala	CAT his	1440 (437)		
frameshift site																						
TTC phe	GGG gly	GTG val	GAG glu	GAG glu	GTC val	GTC val	CTC leu	GTC val	CTG leu	GAG glu	GGA gly	GAA glu	AAA lys	AAA lys	AGC ser	CTG leu	AGC ser	CCA pro	AGG arg	1500 (457)		
CCC pro	CGC arg	CCG pro	GCC ala	CCA pro	CCT pro	CCT pro	GAA glu	GCG ala	CCC pro	GCA ala	CCC pro	CCG pro	GGC gly	CCT pro	CCC pro	GAG glu	GAG glu	GAG glu	GTA val	1560 (477)		
GAG glu	GCG ala	GAG glu	GAA glu	GCG ala	GCG ala	GAG glu	GAG glu	GCC ala	CCG pro	GAG glu	GAG glu	GCC ala	TTG leu	AGG arg	CGG arg	GTG val	GTC val	CGC arg	CTC leu	1620 (497)		
CTG leu	GGG gly	GGG gly	CGG arg	GTG val	CTC leu	TGG trp	GTG val	CGG arg	CGG arg	CCC pro	AGG arg	ACC thr	CGG arg	GAG glu	GCG ala	CCG pro	GAG glu	GAG glu	GAA glu	1680 (517)		
CCC pro	CTG leu	AGC ser	CAA gln	GAC asp	GAG glu	ATA ile	GGG gly	GGT gly	ACT thr	GGT gly	ATA ile	TAA *	TGGGGGCATG			ACGCGGACCAC			1740 (529)			
CGACCTCGGA			CAAGAGACCG			TGGACAACAT			CCTCAAGCGC			CTCCGCCGTA			TTGAGGGCCA			1820				
GGTGCGGGGG			CTCCAGAAGA			TGGTGGCCGA			GGGCCGCCCC			TGCGACGAGG			TCCTCACCCA			1880				
GATGACCGCC			ACCAAGAAGG			CCATGGAGGC			GGCGGCCACC			CTGATCCTCC			ACGAGTTCCT			1940				
GAACGTCTGC			GCCGCCGAGG			TCTCCGAGGG			CAAGGTGAAC			CCCAAGAAGC			CCGAGGAGAT			2000				
CGCCACCATG			CTGAAGAACT			TCATCTA																2027

Figure 4B

GTG AGC GCC CTC TAC CGC CGC TTC CGC CCC CTC ACC TTC CAG GAG GTG GTG 51  
 GGG CAG GAG CAC GTG AAG GAG CCC CTC CTC AAG GCC ATC CGG GAG GGG AGG CTC GCC CAG 111  
 GCC TAC CTC TTC TCC GGG CCC AGG GGC GTG GGC AAG ACC ACC ACG GCG AGG CTC CTC GCC 171  
 ATG GCG GTG GGG TGC CAG GGG GAA GAC CCC CCT TGC GGG GTC TGC CCC CAC TGC CAG GCG 231  
 GTG CAG AGG GGC GCC CAC CCG GAC GTG GTG GAC ATT GAC GCC GCC AGC AAC AAC TCC GTG 291  
 GAG GAC GTG CGG GAG CTG AGG GAA AGG ATC CAC CTC GCC CCC CTC TCT GCC CCC AGG AAG 351  
 GTC TTC ATC CTG GAC GAG GCC CAC ATG CTC TCC AAA AGC GCC TTC AAC GCC CTC CTC AAG 411  
 ACC CTG GAG GAG CCC CCG CCC CAC GTC CTC TTC GTC TTC GCC ACC ACC GAG CCC GAG AGG 471  
 ATG CCC CCC ACC ATC CTC TCC CGC ACC CAG CAC TTC CGC TTC CGC CGC CTC ACG GAG GAG 531  
 GAG ATC GCC TTT AAG CTC CGG CGC ATC CTG GAG GCC GTG GGG CGG GAG GCG GAG GAG GAG 591  
 GCC CTC CTC CTC CTC GCC CGC CTG GCG GAC GGG GCC CTT AGG GAC GCG GAA AGC CTC CTG 651  
 GAG CGC TTC CTC CTC CTG GAA GGC CCC CTC ACC CGG AAG GAG GTG GAG CGC GCC CTA GGC 711  
 TCC CCC CCA GGG ACC GGG GTG GCC GAG ATC GCC GCC TCC CTC GCG AGG GGG AAA ACG GCG 771  
 GAG GCC CTG GGC CTC GCC CGG CGC CTC TAC GGG GAA GGG TAC GCC CCG AGG AGC CTG GTC 831  
 TCG GGC CTT TTG GAG GTG TTC CGG GAA GGC CTC TAC GCC GCC TTC GGC CTC GCG GGA ACC 891  
 CCC CTT CCC GCC CCG CCC CAG GCC CTG ATC GCC GCC ATG ACC GCC CTG GAC GAG GCC ATG 951  
 GAG CGC CTC GCC CGC CGC TCC GAC GCC TTA AGC CTG GAG GTG GCC CTC CTG GAG GCG GGA 1011  
 AGG GCC CTG GCC GCC GAG GCC CTA CCC CAG CCC ACG GGC GCT CCT TCC CCA GAG GTC GGC 1071  
 CCC AAG CCG GAA AGC CCC CCG ACC CCG GAA CCC CCA AGG CCC GAG GAG GCG CCC GAC CTG 1131  
 CGG GAG CGG TGG CGG GCC TTC CTC GAG GCC CTC AGG CCC ACC CTA CGG GCC TTC GTG CGG 1191  
 GAG GCC CGC CCG GAG GTC CGG GAA GGC CAG CTC TGC CTC GCT TTC CCC GAG GAC AAG GCC 1251  
 TTC CAC TAC CGC AAG GCC TCG GAA CAG AAG GTG AGG CTC CTC CCC CTG GCC CAG GCC CAT 1311  
 TTC GGG GTG GAG GAG GTC GTC CTC GTC CTG GAG GGA GAA AAA AAA AGC CTG AGC CCA AGG 1371  
 CCC CGC CCG GCC CCA CCT CCT GAA GCG CCC GCA CCC CCG GGC CCT CCC GAG GAG GAG GTA 1431  
 GAG GCG GAG GAA GCG GCG GAG GAG GCC CCG GAG GAG GCC TTG AGG CGG GTG GTC CGC CTC 1491  
 CTG GGG GGG CGG GTG CTC TGG GTG CGG CGG CCC AGG ACC CGG GAG GCG CCG GAG GAG GAA 1551  
 CCC CTG AGC CAA GAC GAG ATA GGG GGT ACT GGT ATA TAA (1590)

Figure 4C

Met ser ala leu tyr arg arg phe arg pro leu thr phe gln glu val val gly gln glu 20  
 his val lys glu pro leu leu lys ala ile arg glu gly arg leu ala gln ala tyr leu 40  
 phe ser gly pro arg gly val gly lys thr thr thr ala arg leu leu ala met ala val 60  
 gly cys gln gly glu asp pro pro cys gly val cys pro his cys gln ala val gln arg 80  
 gly ala his pro asp val val asp ile asp ala ala ser asn asn ser val glu asp val 100  
 arg glu leu arg glu arg ile his leu ala pro leu ser ala pro arg lys val phe ile 120  
 leu asp glu ala his met leu ser lys ser ala phe asn ala leu leu lys thr leu glu 140  
 glu pro pro pro his val leu phe val phe ala thr thr glu pro glu arg met pro pro 160  
 thr ile leu ser arg thr gln his phe arg phe arg arg leu thr glu glu glu ile ala 180  
 phe lys leu arg arg ile leu glu ala val gly arg glu ala glu glu ala leu leu 200  
 leu leu ala arg leu ala asp gly ala leu arg asp ala glu ser leu leu glu arg phe 220  
 leu leu leu glu gly pro leu thr arg lys glu val glu arg ala leu gly ser pro pro 240  
 gly thr gly val ala glu ile ala ala ser leu ala arg gly lys thr ala glu ala leu 260  
 gly leu ala arg arg leu tyr gly glu gly tyr ala pro arg ser leu val ser gly leu 280  
 leu glu val phe arg glu gly leu tyr ala ala phe gly leu ala gly thr pro leu pro 300  
 ala pro pro gln ala leu ile ala ala met thr ala leu asp glu ala met glu arg leu 320  
 ala arg arg ser asp ala leu ser leu glu val ala leu leu glu ala gly arg ala leu 340  
 ala ala glu ala leu pro gln pro thr gly ala pro ser pro glu val gly pro lys pro 360  
 glu ser pro pro thr pro glu pro pro arg pro glu glu ala pro asp leu arg glu arg 380  
 trp arg ala phe leu glu ala leu arg pro thr leu arg ala phe val arg glu ala arg 400  
 pro glu val arg glu gly gln leu cys leu ala phe pro glu asp lys ala phe his tyr 420  
 arg lys ala ser glu gln lys val arg leu leu pro leu ala gln ala his phe gly val 440  
 glu glu val val leu val leu glu gly glu lys lys ser leu ser pro arg pro arg pro 460  
 ala pro pro pro glu ala pro ala pro pro gly pro pro glu glu glu val glu ala glu 480  
 glu ala ala glu glu ala pro glu glu ala leu arg arg val val arg leu leu gly gly 500  
 arg val leu trp val arg arg pro arg thr arg glu ala pro glu glu glu pro leu ser 520  
 gln asp glu ile gly gly thr gly ile 529

Figure 4D

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Met ser ala leu tyr arg arg phe arg pro leu thr phe gln glu val val gly gln glu 20
his val lys glu pro leu leu lys ala ile arg glu gly arg leu ala gln ala tyr leu 40
phe ser gly pro arg gly val gly lys thr thr thr ala arg leu leu ala met ala val 60
gly cys gln gly glu asp pro pro cys gly val cys pro his cys gln ala val gln arg 80
gly ala his pro asp val val asp ile asp ala ala ser asn asn ser val glu asp val 100
arg glu leu arg glu arg ile his leu ala pro leu ser ala pro arg lys val phe ile 120
leu asp glu ala his met leu ser lys ser ala phe asn ala leu leu lys thr leu glu 140
glu pro pro pro his val leu phe val phe ala thr thr glu pro glu arg met pro pro 160
thr ile leu ser arg thr gln his phe arg phe arg arg leu thr glu glu glu ile ala 180
phe lys leu arg arg ile leu glu ala val gly arg glu ala glu glu glu ala leu leu 200
leu leu ala arg leu ala asp gly ala leu arg asp ala glu ser leu leu glu arg phe 220
leu leu leu glu gly pro leu thr arg lys glu val glu arg ala leu gly ser pro pro 240
gly thr gly val ala glu ile ala ala ser leu ala arg gly lys thr ala glu ala leu 260
gly leu ala arg arg leu tyr gly glu gly tyr ala pro arg ser leu val ser gly leu 280
leu glu val phe arg glu gly leu tyr ala ala phe gly leu ala gly thr pro leu pro 300
ala pro pro gln ala leu ile ala ala met thr ala leu asp glu ala met glu arg leu 320
ala arg arg ser asp ala leu ser leu glu val ala leu leu glu ala gly arg ala leu 340
ala ala glu ala leu pro gln pro thr gly ala pro ser pro glu val gly pro lys pro 360
glu ser pro pro thr pro glu pro pro arg pro glu glu ala pro asp leu arg glu arg 380
trp arg ala phe leu glu ala leu arg pro thr leu arg ala phe val arg glu ala arg 400
pro glu val arg glu gly gln leu cys leu ala phe pro glu asp lys ala phe his tyr 420
arg lys ala ser glu gln lys val arg leu leu pro leu ala gln ala his phe gly val 440
glu glu val val leu val leu glu gly glu lys lys lys pro asp pro lys ala pro pro 460
gly pro thr ser 464

```

Figure 4E



Met	ser	ala	leu	tyr	arg	arg	phe	arg	pro	leu	thr	phe	gln	glu	val	val	gly	gln	glu	20
his	val	lys	glu	pro	leu	leu	lys	ala	ile	arg	glu	gly	arg	leu	ala	gln	ala	tyr	leu	40
phe	ser	gly	pro	arg	gly	val	gly	lys	thr	thr	thr	ala	arg	leu	leu	ala	met	ala	val	60
gly	cys	gln	gly	glu	asp	pro	pro	cys	gly	val	cys	pro	his	cys	gln	ala	val	gln	arg	80
gly	ala	his	pro	asp	val	val	asp	ile	asp	ala	ala	ser	asn	asn	ser	val	glu	asp	val	100
arg	glu	leu	arg	glu	arg	ile	his	leu	ala	pro	leu	ser	ala	pro	arg	lys	val	phe	ile	120
leu	asp	glu	ala	his	met	leu	ser	lys	ser	ala	phe	asn	ala	leu	leu	lys	thr	leu	glu	140
glu	pro	pro	pro	his	val	leu	phe	val	phe	ala	thr	thr	glu	pro	glu	arg	met	pro	pro	160
thr	ile	leu	ser	arg	thr	gln	his	phe	arg	phe	arg	arg	leu	thr	glu	glu	glu	ile	ala	180
phe	lys	leu	arg	arg	ile	leu	glu	ala	val	gly	arg	glu	ala	glu	glu	glu	ala	leu	leu	200
leu	leu	ala	arg	leu	ala	asp	gly	ala	leu	arg	asp	ala	glu	ser	leu	leu	glu	arg	phe	220
leu	leu	leu	glu	gly	pro	leu	thr	arg	lys	glu	val	glu	arg	ala	leu	gly	ser	pro	pro	240
gly	thr	gly	val	ala	glu	ile	ala	ala	ser	leu	ala	arg	gly	lys	thr	ala	glu	ala	leu	260
gly	leu	ala	arg	arg	leu	tyr	gly	glu	gly	tyr	ala	pro	arg	ser	leu	val	ser	gly	leu	280
leu	glu	val	phe	arg	glu	gly	leu	tyr	ala	ala	phe	gly	leu	ala	gly	thr	pro	leu	pro	300
ala	pro	pro	gln	ala	leu	ile	ala	ala	met	thr	ala	leu	asp	glu	ala	met	glu	arg	leu	320
ala	arg	arg	ser	asp	ala	leu	ser	leu	glu	val	ala	leu	leu	glu	ala	gly	arg	ala	leu	340
ala	ala	glu	ala	leu	pro	gln	pro	thr	gly	ala	pro	ser	pro	glu	val	gly	pro	lys	pro	360
glu	ser	pro	pro	thr	pro	glu	pro	pro	arg	pro	glu	glu	ala	pro	asp	leu	arg	glu	arg	380
trp	arg	ala	phe	leu	glu	ala	leu	arg	pro	thr	leu	arg	ala	phe	val	arg	glu	ala	arg	400
pro	glu	val	arg	glu	gly	gln	leu	cys	leu	ala	phe	pro	glu	asp	lys	ala	phe	his	tyr	420
arg	lys	ala	ser	glu	gln	lys	val	arg	leu	leu	pro	leu	ala	gln	ala	his	phe	gly	val	440
glu	glu	val	val	leu	val	leu	glu	gly	glu	lys	lys	lys	ala							454

Figure 4F

		ATP site	
E.coli	MSYQVLARKWRPQTFADVVGQEHVLTALANGLSLGRIHHAYLFSGTRGVGKTSIARLLAK	60	
H.inf.	.....K.....II.....KDN.L.....F..	60	
B.sub.	...A.Y.VF...R.E.....ITKT.Q.A.LQKKFS.....P..T...A.KIF..	60	
C.cres.	DA.T.....Y..R..E.LI...AMVRT...AF.T...A..FMLT.V.....TT.....R	113	
M.gen.	-MH..FYQ.Y..IN.KQTL...SIRKI.V.AINRDKLPNG.I...E..T...TF.KII..	59	
T.th.	--VSA.Y.RF..L..QE.....KEP.LKAIRE..LAQ.....P.....TT.....M	58	
		Zn <sup>++</sup> finger	
		* * *	
E.coli	GLNCET---GITATPCGVCDNCREIEQGRFVDLIEIDAASRTKVEDTRDLLDNVQYAPA	116	
H.inf.	...VH---.V.....E.E..KA...N.I.....E.....K.V	116	
B.sub.	AV...H---APVDE..NE.AA.KG.TN.SIS.V.....NNG.DEI..IR.K.KF..S	116	
C.cres.	A..Y..DTVK.PSVDLTTEGYH..S.IE..HM.VL.L.....DEM.E...G.R...V	173	
M.gen.	AI..LN---WDQIDV.NS..V.KS.NTNSAI.IV.....KNGIN.I.E.VE..FNH.F	115	
T.th.	AVG.QG-----EDP.....PH.QAVQR.AHP.VVD.....NNS...V.E.RERHL..L	112	
E.coli	RGRFKVYLIDEVHMLSRHSFNALLKTLEEPPEHVKFLLATTPQKLPVTILSRCLQFHLK	176	
H.inf.	V.....Y.....	176	
B.sub.	AVTY...I.....IGA.....CI.I...E.H.I.L..I..QR.DF.	176	
C.cres.	EA.Y...I.....TAA.....P.A..IF...EIR.V.....QR.D.R	233	
M.gen.	TFKK...IL..A...TTQ.WGG.....S.PY.L.IFT..EFN.I.L.....QS.FF.	175	
T.th.	SAPR..FIL..A...KSA.....P..L.VF...E.ERM.P.....TQH.RFR	172	
E.coli	ALDVEQIRHQLEHILNEEHIAHEPRALQLLARAAEGSLRDALSLTDQAIASGDGQ--VST	234	
H.inf.	...ET..SQH.A...TQ.N.PF.DP..VK..K..Q..I..S.....M..R.--.TN	234	
B.sub.	RITSQA.VGRMNK.VDA.QLQV.EGS.EII.S..H.GM.....L....SFSGDI--LKV	234	
C.cres.	RVEPDVLVKHFDR.SAK.GARI.MD..A.I.....V..G...L...VQTERGQT.TS	293	
M.gen.	KITSDL.LER.ND.AKK.K.KI.KD..IKI.DLSQ.....G...L..LAI.LIVKKL.LL	235	
T.th.	R.TE.E.AFK.RR..EAVGREA.EE..L...L.D.A...E..LERFLLLEGP---LTR	229	
E.coli	QAVSAMLGTLDLDDQALSLVEAMVEANGERVMA LINEAAARGIEWEALLVEMLGLLHRIAM	294	
H.inf.	NV..N...L...NYSVDILY.LHQG...LL.RTLQRV.DAAGD.DK..G.CAEK..Q..L	294	
B.sub.	EDALLIT.AVSQLYIGK.AKSLHDK.VSDALETL..LLQQ.KDPAK.IED.IFYFRDMLL	294	
C.cres.	TV.RD...LA.RS.TIA.Y.HVMAGKTKDALEGFRALWGF.ADPVVMLDV.DHC.AS.V	353	
M.gen.	MLKKHLISLIEMQNL.L.KQFYQ.I	260	
T.th.	KE.ERA..SPPGTGVAEIAASLARGKTAEALG.ARRLYGE.YAPRS.VSGL.EVFREGLY	289	

Figure 5

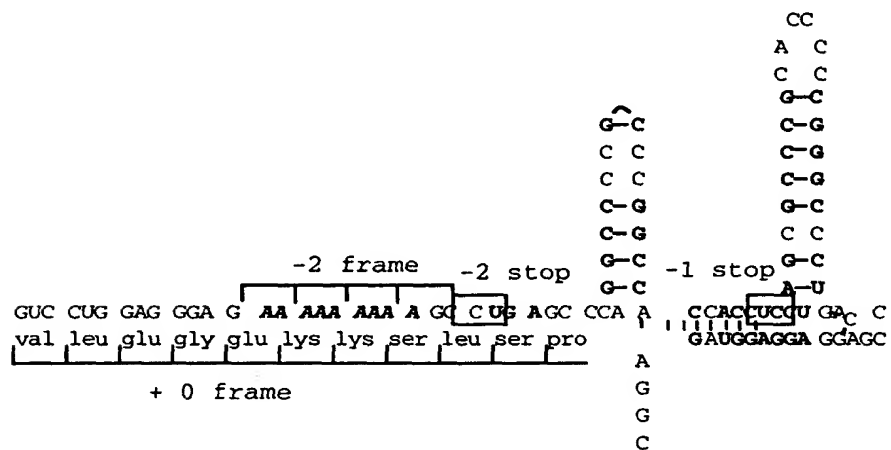


Figure 6

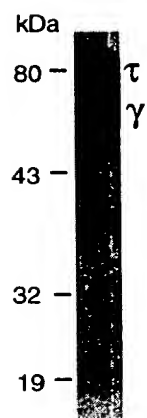
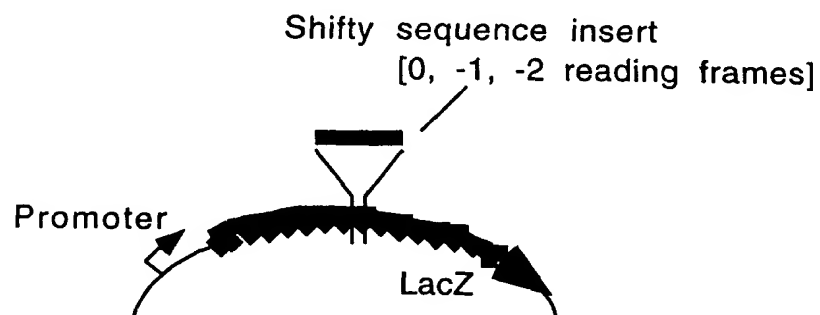


Figure 7



	Reading frame	Blue	White
Shifty sequence	0	+	
	- 1	+	
	- 2	+	
Mutant sequence	0	++	
	- 1		+
	- 2		+

Figure 8

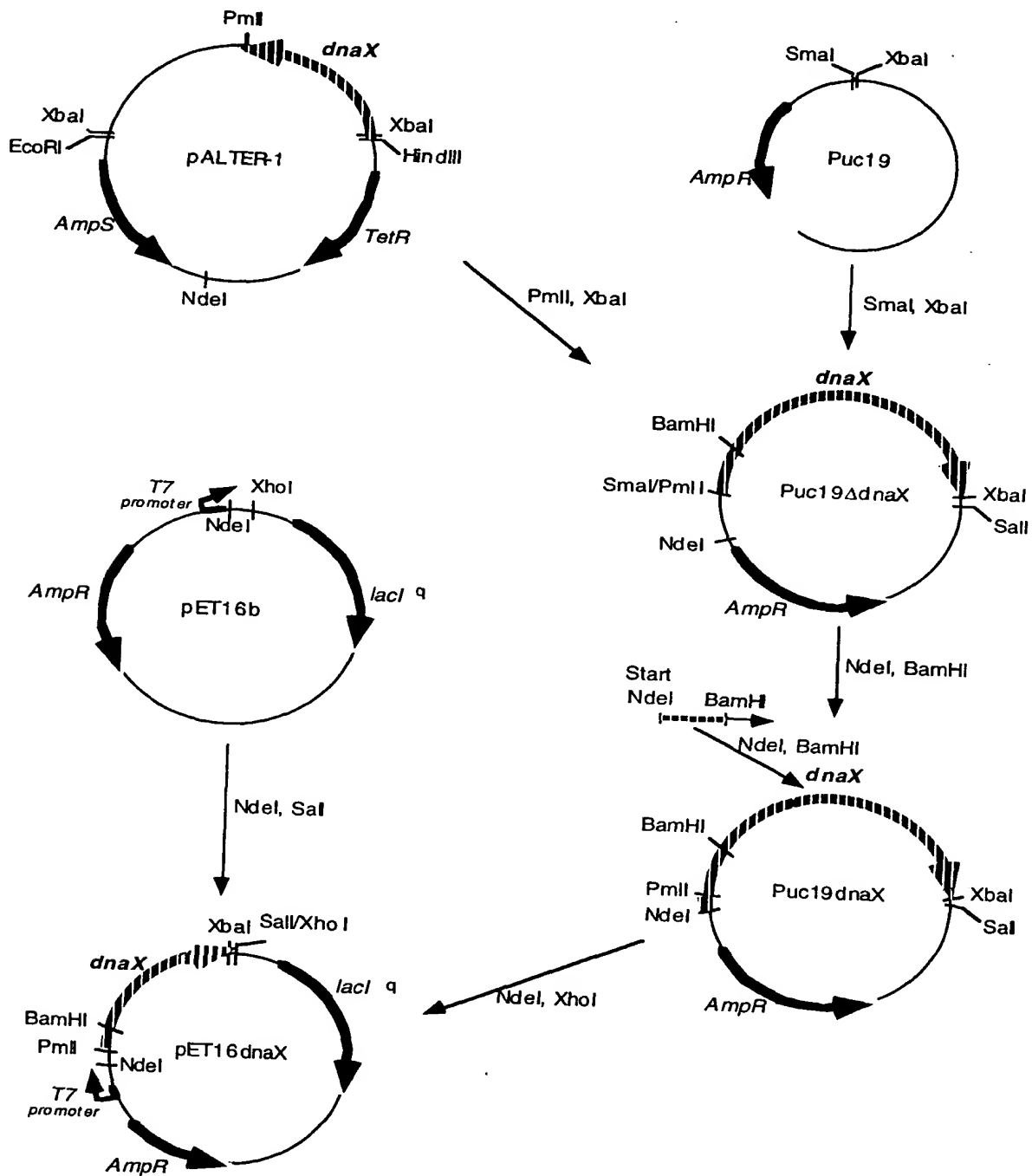


Figure 9

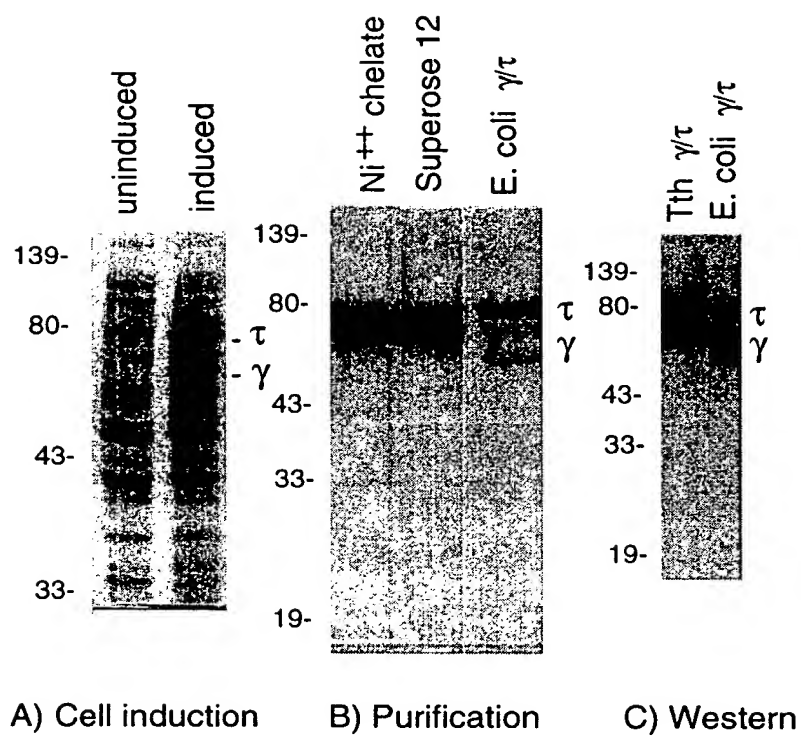


Figure 10

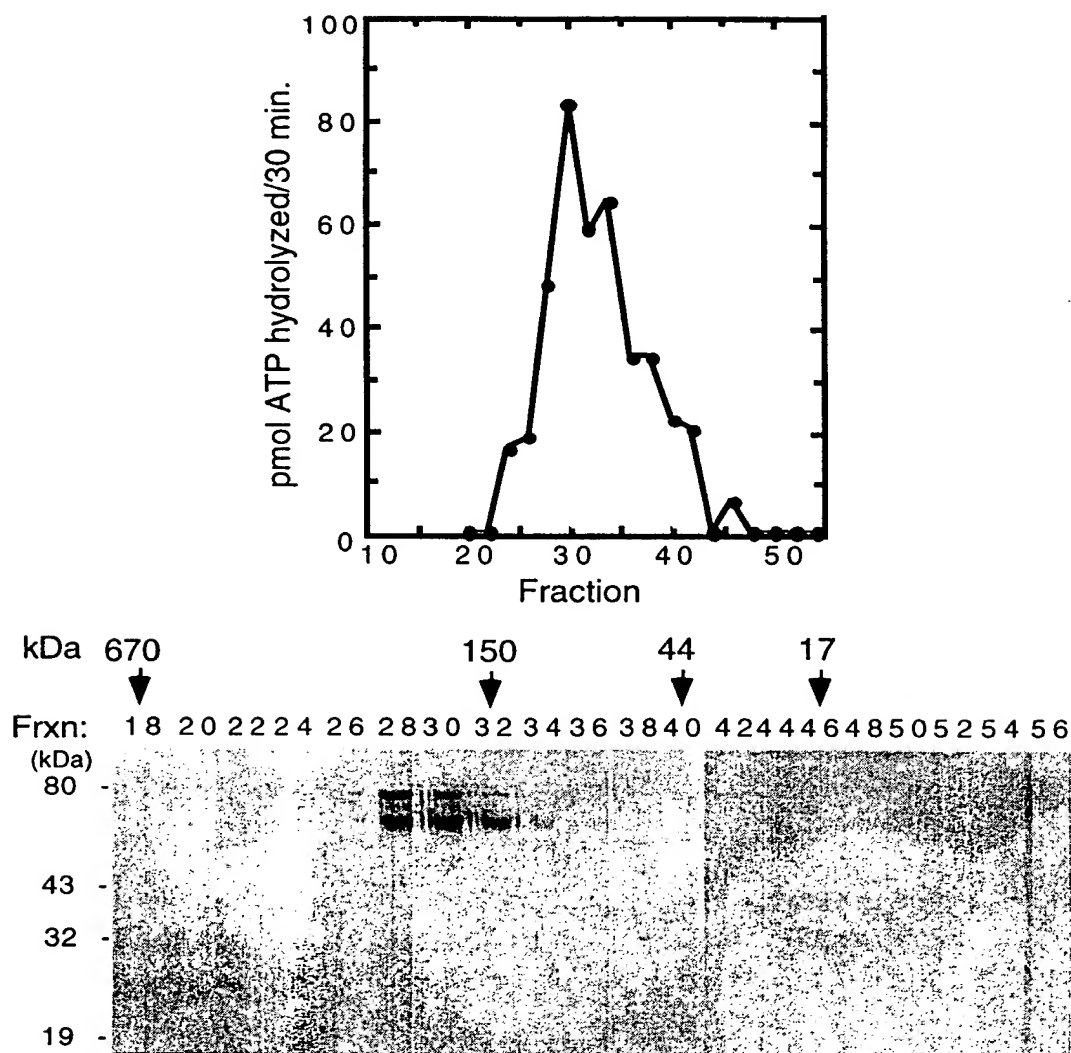


Figure 11



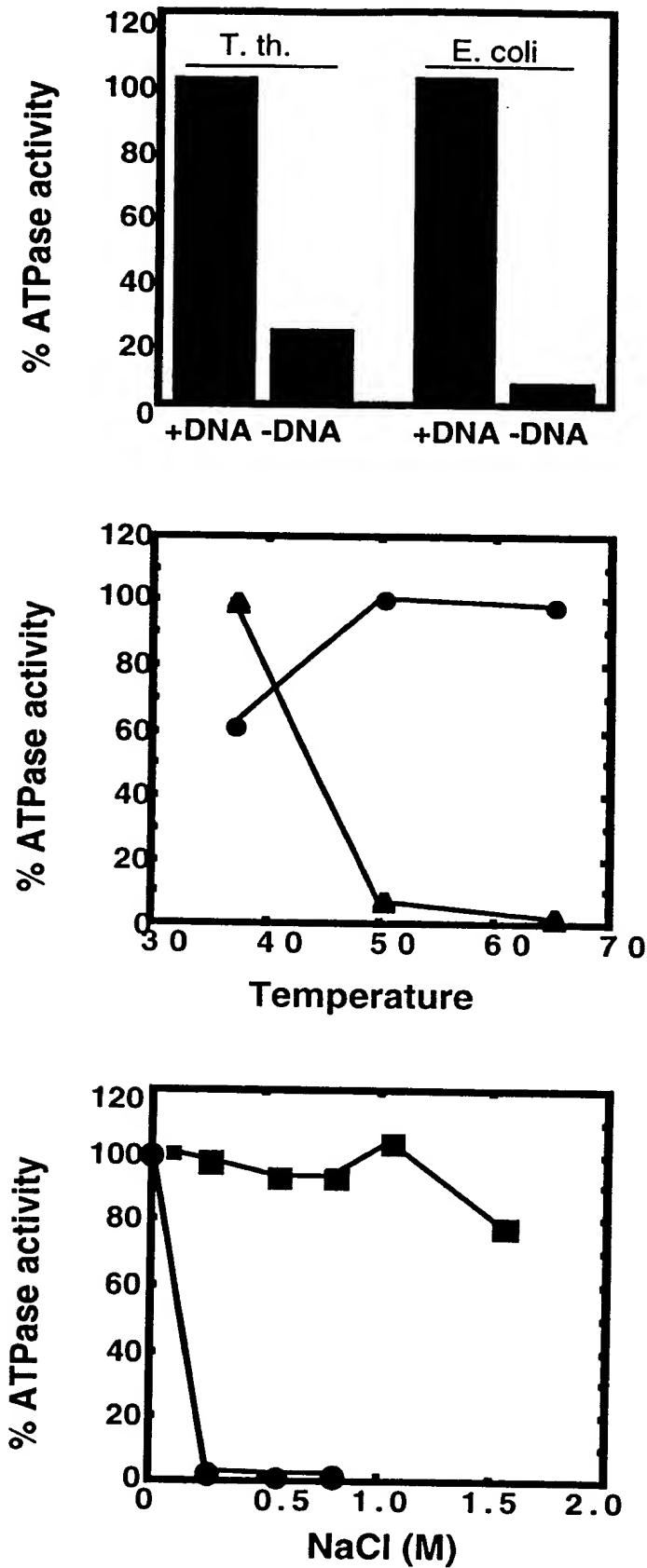
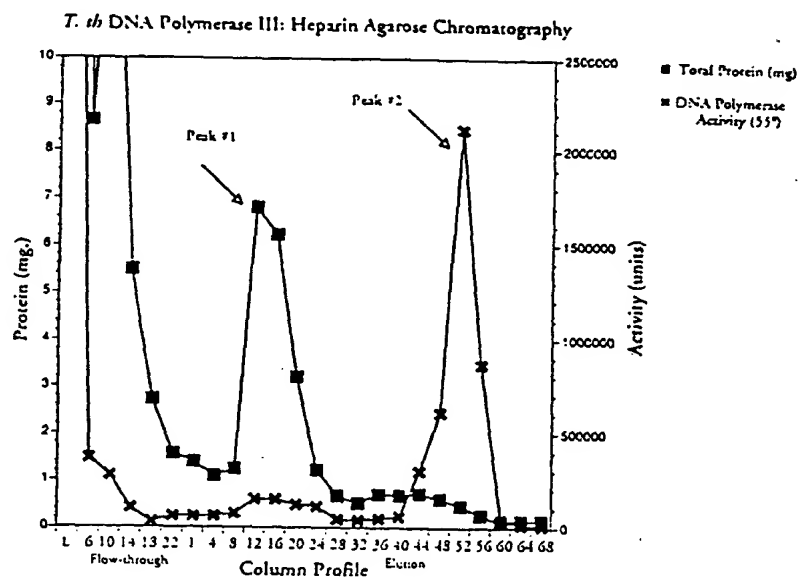


Figure 12

A)



B) ATP Agarose Step Column

C)

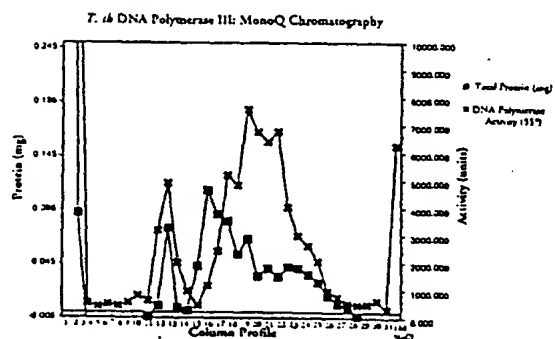
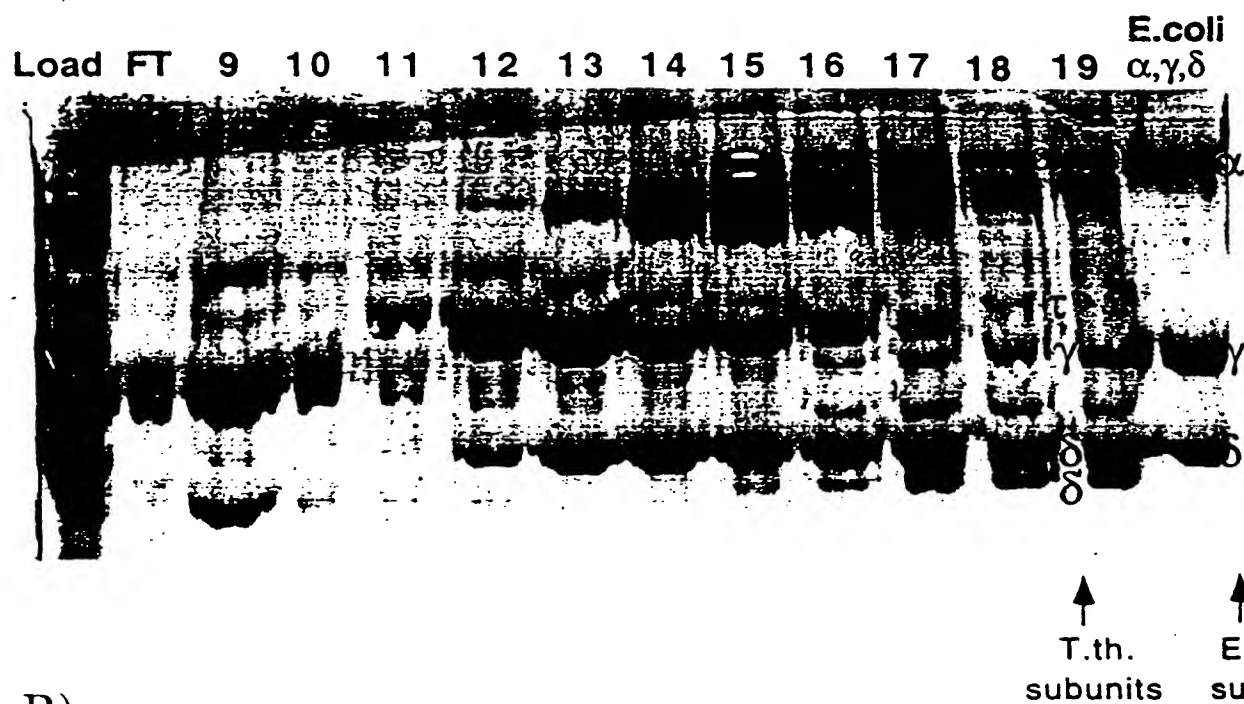


Figure 13

A)



B)

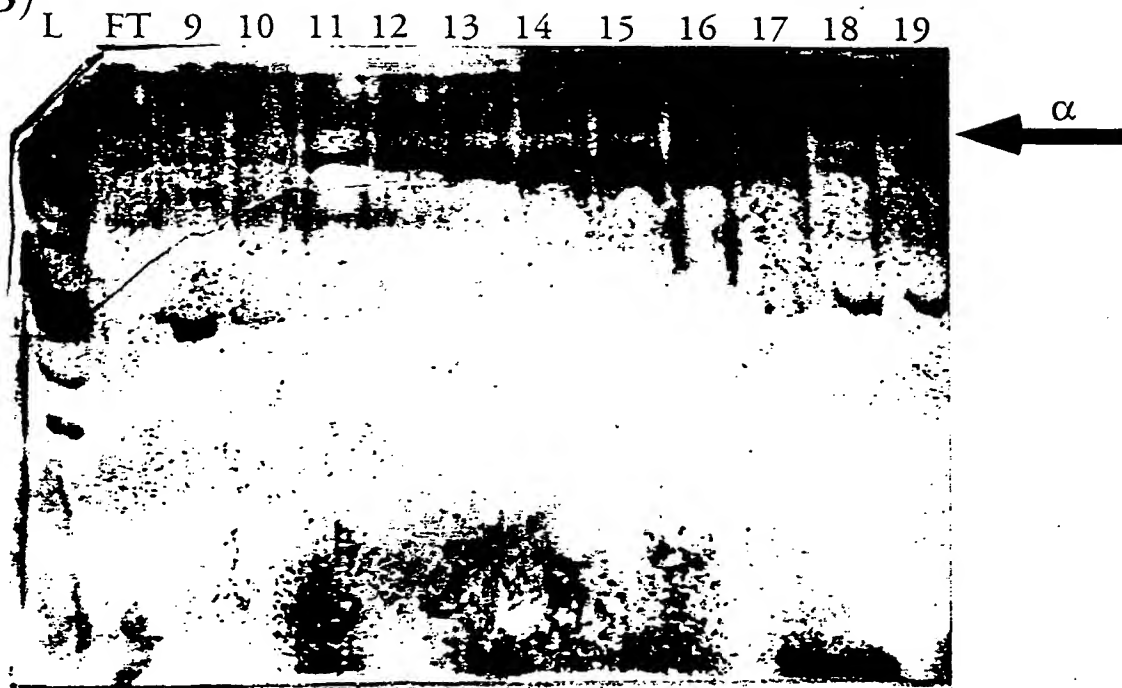


Figure 14

## A) Alignment of TTH1 with alphas subunits of other organisms.

E.coli	DRYFLELIRTGRPDEESYLHAAVELAEARGLPVV	197	(ID#72)
V.chol.	DHFYLELIRTGRADEESYLHFALDVAEQYDLPVV	197	(ID#73)
H.inf.	DHFYLALSRTGRPNEERYIQAALKLAERCDLPLV	197	(ID#74)
R.prow.	DRFYFEIMRHDLPPEEQFIENSYIQIASELSIPIV	195	(ID#75)
H.pyl.	DDFYLEIMRHGILDQRFIDEQVIKMSLETGLKII	213	(ID#76)
S.sp.	DDYYLEIQDHGSVEDRLVNINLVKIAQELDIKIV	202	(ID#77)
M.tub.	DNYFLELMDHGLTIERRVRDGLLEIGRALNIPPL	220	(ID#78)
T.th.	FFIEIQNHGLSEQK		(ID#61)

## B) Alignment of TTH2 with alphas subunits of other organisms.

E.coli	NKRRAKNGEPPLDIAAIPLDDKKSFDMLQRSETTAVFQLESRGMKD	618	(ID#79)
V.chol.	NPRLKKAGKPPVRIEAIPLDDARSFRNLQDAKTTAVFQLESRGMKE	618	(ID#80)
H.inf.	NVRMVREGKPRVDIAAIPLDDPESFELLKRSETTAVFQLESRGMKD	618	(ID#81)
R.prow.	CKKLLKEQGIKIDFDDMTFDDKKTQMLCKGKGVGVFQFESIGMKD	624	(ID#82)
H.pyl.	LKIIKTQHKISVDFLSLDMDDPKVYKTIQSGDTVGIQFQIES-GMFQ	648	(ID#83)
S.sp.	QERKALQIRARTGSKKL PDDVKKTHKLEAGDLEGIFQLESQGMKQ	643	(ID#84)
M.tub.	IDNVRANRGIDLDESVP LDDKATYELLGRGDTLGVFQLDGGPMRD	646	(ID#85)
T.th.	RVELDYDALTLDD		(ID#60)

Figure 15

A)

Start codon

ATGGGCGGGAGCTCCGCTTCGCCCACCTCCACCAGCACA  
CCCAGTTCTCCCTCCTGGACGGGGCGCCGAAGCTTTCCGA  
CCTCCTCAAGTGGGTGGAGGAGACGACCCCGAGGACCCC 120  
GCCTTGGCCATGACCGACCACGGCAACCTCTTCGGGGCCG  
TAGAGTTCTACAAGAAGGCCGCCGAAATGGGCATCGAGCC  
CATCCTGGGTACGAGGCCTTACGTGGCGGCGGAAAGCCCG 240  
TTTGACCGCAAGCGGGGAAAGGGCCTAGACGGGGGCTACT  
TTCACCTCACCTCCTCGCCAAGGACTTCACGGGGTACCA  
GAACCTGGTGCGCCTGGCGAGCCGGGCTTACCTGGAGGGG 360  
TTTTACGAAAAGCCCCGGATTGACCGGGAGATCCTGCGCG  
AGCGCCGAGGGCCTCATCGCCTCTCGGGGTGCCTCGGGGC  
GGAGATCCCCCAGTTTCATCCTCCAGGACCGTCTGGACCTG 480  
GCCGAGGCCCCGGCTCAACGAGGACCTCTCCATCTTCAAGG  
ACCGCTTCTTCATTACATCCAGAACCACGGCCTCCCCGA  
GCAGAAAAAGTCAACGAGGTCCCTCAAGGAGTTCGCCCCG 600  
AAGTACGGCCTGGGGATGGTGGCCACCAACGACGGCCATT  
ACGGGAGGAAGGAGGCCCGCAGCGCCACGAGGTTTTCCT  
CGCCATCCAGTCCAAGAGCACCTTGGACGACCCCGGGGCC 720  
GTTGGCTTTCCCCCTGCGGGAGTTCTACGTGAAGACCCCCG  
AGGAGACGTGCGGGCCGGTGTTCCTCGAGGAGGAGTGGGG  
GGACGAGCCCTTTGACAACACCGTGGAGATCGCCCGCATG 840  
TGCAACGTGGAGCTGCCCATCGGGACAAGATGGTCTACCC  
GAATCCCCCGCTTCCCCCTCCCCGAGGGACCGGGGACCGA  
GGCCAAGTACCTAATGGAGCTAACCTTCAAGGGGGCCCTC 960  
CGCCGTTACCCGGACCGAATCACCGAGGGTTTCTACCGGG  
AGGTTTTCGCCCTTTTGGGGAAGCTTCCCCCCCACGGGCA  
CGGGGAGGCCTTGGCCGAGGCCTTGGCCCAGGTGGAGCGG 1080  
GAGGCTTGGGAGAGGCTCATGAAGAGCCTCCCCCCTTG  
ACCGGGTCCAAGGAGTTCCA

B)

MGRELRFAPHLHQHTQFSLLDGAPKLSDLLKWVEETTPEDP  
ALAMTDHGNLFGAVEFYKKAEMGIEPILGTRPYVAAESP  
FDRKRKGKLDGGYFHLTLLAKDFTGYQNLVRLASRAYLEG 120  
FYEKPRIDREILRERRGPHRLSGCLGAEIPQFILQDRLDL  
**FFIEIQNHGLSEQK**  
AEARLNEDLSIFKDRFFIHIQNHGLPEQKKVNEVLKEFAR  
KYGLGMVATNDGHYGRKEARSAHEVFLAIQSKSTLDDPGA 240  
VGFPLREFYVKTPEETCGPVFPPEEWGDEPFDNTVEIARM  
CNVELPIGTRWSTRIPRFPLPEGPGTEAKYLMELTFKGPL  
RRYPDRITEGFYREVFRLLGKLPPHGHGEALAEALAQVER 360  
EAWERLMKSLPPFDRGPRSS

Figure 16

	Start1	Start2	3'-Exo I
T.th.	VERVVRTLLDGRFLLEEGVGLWEWRYPPFLEGEAVVVLDLETTGLAG-----LDEVIEVGLLRLEGG---RRLPF		
D.rad.		PWPQDVVVFDLETTGFSPA-----SAAIVEIGAVRIVGGQIDETLKF	
Bac.sub.	HGIKMIYGMEANLVDDGVPIAYNAHRLLEEETYYVVFVDTTGLSAV-----YDTIIELA AVKVKGGE--IIDKF		
H.inf.		MINPNRQIVLDTETTGMNQLGAHYEGHCHIEIGAVELINRR-YTGNNX	
E.c.		MSTAITRQIVLDTETTGMNQIGAHSEGHKIIIEIGAVEVNNRR-LTGNNF	
H.pyl.	NLEYLKACGLNFIETSENLITLKNLKTPLKDEVFSPIDLETTGSCPI-----KHEILEIGAVQVKGGE--IINRF		

	3'-Exo II
T.th.	QSLVR-PLPP---AEARSWNLT--GIPREALEEAPSLEEVLKAYPLRGDATLVIHNAAFDLGFL-RPALEGLG
D.rad.	ETLVR-PTRPDGSMLSIPWQAQRVHGISEMVRRAPAXKDVLPDFDFVDGSAVVAHNVSFDGGFM-RAGAERLG
Bac.sub.	EAFAN-PHRP---LSATIIELT--GITDDMLQDAPDVVDVIRDFREWIGDDILVAHNASFDMGFL-NVAYKKLL
H.inf.	HIYIK-PDRP---XDPDAIKVH--GITDEMLADKPEFKEVAQDFLDYINGAELLIHNAFPDVGFM-DYEFKRLN
E.c.	HVYLK-DRLV----DPEAFGVH--GIAVDFLDKPTFAEVAVEFMDYIRGAELVIHNAAFDIGFM-DYEFSLK
H.pyl.	ETLVKVKVSP-----DYIAELT--GITYEDTLNAPSAHEALQELRLFLGNSVFAHNAFNDYNFLGRYFVEKLH

	3'-Exo IIIC
T.th.	-----YRLNPVVDLSRLARRGLPGLRRYGLDALSEVLELPRRT--CHRALEDVERTLAVVHEVYYMLT-----SG
D.rad.	----LSWAPERELCTMQLSRRAFP RERTHNLTVLAERLGLFAPGGRHRSYGDVQVTAQAYLRLLLELLG-----ER
Bac.sub.	E---VEKAKNPVIDTLELGRFLYPEFKNHRNLTLCKKFDIELTQ--HHRAIYDTEATAYLLLKMLKDAA-----EK
H.inf.	-LNVKTDDICLVTDTLQMARQMPGKRN-NLDALCDRLGIDNSKRTLHGALLDAEILADVYLMMTGGQTNLFDEEE
E.c.	RDIAKTNTFCVTDLSLAVARKMFPKGKRN-SLDALCARYEIDNSKRTLHGALLDAQILA EVYLAMTGGQTSMAFAME
H.pyl.	-----CPLLNLKLCITLDSLKRAILSMRY-SLSFLKELLGFGIEV--SHRAYADALASYKLF EICLLNLP--SYIKT

Figure 17

A)

```

ATGGTGGAGCGGGTGGTGCGGACCCCTTCTGGACGGGAGGT 40
TCCTCCTGGAGGAGGGGGTGGGGCTTTGGGAGTGGCGCTA
CCCCCTTCCCCTGGAGGGGGAGGCGGTGGTGGTCCCTGGAC 120
CTGGAGACCACGGGGCTTGCCGGCCTGGACGAGGTGATTG
AGGTGGGCCTCCTCCGCCTGGAGGGGGGAGGCGCCTCCC 200
CTTCCAGAGCCTCGTCCGGCCCCCTCCCCGCCCGCCGAAGCC
CGTTCGTGGAACCTCACCGGCATCCCCGGGAGGCCCTGG 280
AGGAGGCCCCCTCCCCTGGAGGAGGTTCTGGAGAAGGCCTA
CCCCCTCCGCGGCGACGCCACCTTGGTGATCCACAACGCC 360
GCCTTTGACCTGGGCTTCTCCGCCCCGGCCTTGGAGGGCC
TGGGCTACCGCCTGGAAAACCCCGTGGTGGACTCCCTGCG 440
CTTGGCCAGACGGGGCTTACCAGGCCTTAGGCGCTACGGC
CTGGACGCCCTCTCCGAGGTCCTGGAGCTTCCCCGAAGGA 520
CCTGCCACCGGGCCCTCGAGGACGTGGAGCGCACCCCTCGC
CGTGGTGCACGAGGTATACTATATGCTTACGTCCGGCCGT 600
CCCCGCACGCTTTGGGAACTCGGGAGGTAG

```

B)

```

MVERVVRTLLDGRFLLEEGVGLWEWRYPPFLEGEAVVVD 40
LETTGLAGLDEVIEVGLLRLEGGRRLPFQSLVRPLPPAEA
RSWNLTGIPREALEEAPSLEEVLEKAYPLRGDATHVIHNA 120
AFDLGFLRPALEGLGYRLENPVVDSLRLARRGLPGLRRYG
LDALSEVLELPRRTCHRALEDVERTLAVVHEVYYMLTSGR 200
PRTLWELGRZ

```

Figure 18

## Alignment of dnaA genes.

P.mar.	MLEASWEK	VQSSL--KQNLK--	-----PSYE	TWIRPTEFSG--FKN	GELTLIAPNSFSSAW	LKNYSQTIQETAE-	65	
Syn.sp.	MVSCENLWQQ	ALAIL--ATQLTK--	-----PAFD	TWIKASVLIS--LGD	GVATIQVENGFLVNH	LQKSYGPLLMEVLT-	67	
B.sut.	MENILDLWNQ	ALAQI--EKKLSK--	-----PSFE	TWMKSTKAHS--LQG	DTLTITAPNEFARDW	LESRYLHLIADTIY-	67	
M.tub.	MTDDPGSGFTTVWNA	VVSELNGDPKVVDDGP	SSDANLSAPLTPQQR	AWLNLVQPLT--IVE	GFALLSVPSFVQNE	IERHLRAPITDALS-	87	
T.th.	MSHEAVWQH	VLEHI--RRSITE--	-----VEFH	TWFERIRPLG--IRD	GVLELAVPTSFALDW	IRRHVAGLIQEGPR-	66	
E.coli	MSLSLWQQ	CLARL--QDELP--	-----TEFS	MWIRPLQAE--LSD	NTLALYAPNRFVLWD	VRDKYLNNINGLLT-	64	
T.mar.	MKER	ILQEI--KTRVNR--	-----KSWE	LWFSSFDVKS--IEG	NKVVFSVGNLFIKEW	LEKKYYSVLKSAVK-	61	
H.pyl.	MDTNNNIEKE	ILALVKQNPKVS-	-----IEYE	NYFSQLKYNPNASKS	DIAFFYAPNQVLCTT	ITAKYGALLKEILSQ	72	
P.mar.	EIFG---EPVTVHVK	VKANAESSDEHYSSA	P-----	---ITPPLEASPGSV	DSSGSSLRLSK----	-KTLPLNLRYVFN	130	
Syn.sp.	DLTG---QEITVKLI	TDGLEPHS---LIGQ	E-----	---SSLPMETTP----	-----	-KNATALNGKYTFSR	115	
B.sut.	ELTG---EELSIFV	IPQNQDVEDFMPKPQ	VKKAVKEDTSDFPQN	-----	-----	-----MLNPKYTFDT	119	
M.tub.	RRLGH-QIQLGVRIA	PPATDEADDITVPPS	ENPATTSPTDTTNDND	EIDDSAAAARGDNQHS	WPSYFTERPHNTDSA	TAGVTSLNRRYTFDT	176	
T.th.	LLGAQ-APRFELRVV	PGVVVQEDIFQPPPS	PPAQAP-	-----	-----	-----EDTFKT	108	
E.coli	SFCGADAPQLRFEVG	TKPVTQTPOAAVTSN	VAAPAQVAQTQPORA	APSTRSGWDNV	PAPA	EP-----	-TYRSNVNVKHTFDN	140
T.mar.	VVLG---NDATFEIT	YEAPEHSSSYSEPLV	KKRAVLLTP----	-----	-----	-----LNPDYTFEN	106	
H.pyl.	NKVG-MHLAHSVDVR	IEVAPKIQINAQSNI	NYKAIKTS-----	-----	-----	-----VKDSYTFEN	118	
P.mar.	FVVGPNSRMAHAAAM	AVAESPGREFNPFLFI	CGGVGLGKTHLMQAI	GHYRLEIDPGAKVSY	VSTETFTNDLIL--A	IRQDRMQAFDRYR-	217	
Syn.sp.	FVVGPTNRMHAASL	AVAESPGREFNPFLFI	CGGVGLGKTHLMQAI	AHYRLEMYPNAKVY	VSTERFTNDLIT--A	IRQDNMEDFRSYR-	202	
B.sut.	FVIGSGNRFHAASL	AVAEPAPAKAYNPFLFI	YGGVGLGKTHLMHAI	GHYVIDHNPSAKVY	LSSEKFTNEFIN--S	IRDNKAVDFRNRYR-	206	
M.tub.	FVIGASNRFAHAAAL	AIAEAPARAYNPFLFI	WGESGLGKTHLLHAA	GNVYQRLFPQMRVKY	VSTEEFTNDFIN--S	LRDDRKVAFAKRSYR-	263	
T.th.	SWWGPTTPWPHGGAV	AVAESPGRAYNPFLFI	YGGRGLGKTYLMAV	GPLRAKRFPHMRLEY	VSTETFTNELINRPS	AR-DRMTEFRERYR-	196	
E.coli	FVEGKSNQLARAAAR	QVADNPGGAYNPFLFI	YGGTGLGKTHLLHAV	GNGIMARKPNAKVY	MHSERFVQDMVK--A	LQNNAIIEFKRYR-	227	
T.mar.	FVVGPGNSFAYHAAL	EVAKHPGR-YNPLFI	YGGVGLGKTHLLQSI	GNVYVQNEPDLRVMY	ITSEKFLNDLVD--S	MKEGKLENEFREKYR	193	
H.pyl.	FVVGSCNNTVYEIAK	KVAQSDTPPYNPVLF	YGGTGLGKTHILNAI	GNHALEK--HKKVVL	VTSEDFLTDFLK--H	LDNKTMDSFKAKYR-	203	
P.mar.	AADLILVDDIQFIEG	KEYTQEEFFHTFNAL	HDAGSQIVLASDRPP	SQIPRLQERLMSRFS	MGLIADVQAPDLETR	MAILQKKAHERVGL	307	
Syn.sp.	SADFLILDDIQFIK	KEYTQEEFFHTFNAL	HEAGQVVASDRAP	QRIPGLQDRILSRFS	MGLIADIQVPDLETR	MAILQKKAEDRIRL	292	
B.sut.	NVDVLLIDDIQFLAG	KEQTQEEFFHTFNAL	HEESKQIVISSDRPP	KEIPTLEDRLRSRFE	WGLITDITPPDLETR	IAILRKKAKEGLDI	296	
M.tub.	DVDVLLVDDIQFIEG	KEGIQEEFFHTFNAL	HNANKQIVISSDRPP	KQLATLEDRLRTRFE	WGLITDVQPPELETR	IAILRKKAQMERLAV	353	
T.th.	SVDLLLVDDVQFIAG	KERTQEEFFHTFNAL	YEAHKQIILSSDRPP	KDLITLEARLRSRFE	WGLITDNPAPDLETR	IAILKNNAS-SGPED	285	
E.coli	SVDALLIDDIQFFAN	KERSQEEFFHTFNAL	LEGNQIILTSDRYP	KEINGVEDRLKSRFG	WGLTVAIEPPELETR	VAILMKKADENDIRL	317	
T.mar.	KVDILLIDDVQFLIG	KTGVQTELFTFNEL	HDSGKQIVICSDREP	QKLEFQDRLVSRFQ	MGLVAKLEPPDEETR	KSIARKMLEIEHGEL	283	
H.pyl.	HCDFLLDDAQFLQG	KPKLEEEFFHTFNEL	HANSKQIVLISDRSP	KNIAGLEDRLKSRFE	WGITAKVMPDLETK	LSIVKQKCOLNQITL	293	
P.mar.	PRDLIQFIAGRFTSN	IRELEGALTRAIFA	SITGLPMTVDSIAPM	LD----PNGQGEVET	PKQVLDKVAEVFKVT	PDEMRSASRRR-PVS	392	
Syn.sp.	PKEVIEYIASHYTSN	IRELEGALIRAIAYT	SLSNVAMTVENIAPV	LN----PPVEKVAAA	PETIITIVAQHYQLK	VEELLSNSRRR-EVS	377	
B.sut.	PNEVMYLIANQIDSN	IRELEGALIRVVAYS	SLINKDINADLAAEA	LKDII-PSSKPKVIT	IKEIQRVVGQQFNK	LEDFAKAKRTK-SVA	384	
M.tub.	PDDVLELIASSIERN	IRELEGALIRVTAF	SLNKTPIDKALAEIV	LRDLI-ADANTMQIS	AATIMAATAEYFDTT	VEELRGPGKTR-ALA	441	
T.th.	PEDALEYIARQVTSN	IREWEGALMRASPFA	SLNGVELTRAVAACA	LRHLR-P--RELEAD	PLEIIRKAGPVRPE	TPGGAHGERRKKEVV	372	
E.coli	PGEVAFPIAKRLRSN	VRELEGALNRVIANA	NFTGRAITIDFVREA	LRDLL-A-LQEKLV	IDNIQKTVAEYYKIK	VADLLSKRRSR-SVA	404	
T.mar.	PEEVLNFVAENVDDN	LRLRGAI IKLLVYK	ETTQKEVDLKEAILL	LKDFIKPNRVKAMP	IDELIEIVAKVTGVP	REEILSNRSNV-KAL	372	
H.pyl.	PEEVMYIAQHISDN	IRQMEGAI IKISVNA	NLMNASIDLNLAKTV	LEDL--QKDHAEGSS	LENILLAVAQSLNLK	SSEIKVSSRQK-NVA	380	
P.mar.	QARQVGMVLMRQGTN	LSLPRIGDTFGGKDH	TTVMYAIEQVEKKLS	S-----DPQIA	SQVQKIRDLLQIDSR	RKR----	461	
Syn.sp.	LARQVGMVLMRQHTD	LSLPRIGEAFFGGKDH	TTVMYSCDKITQLQQ	K-----DWETS	QTLTSLSHRINIAGQ	APES----	447	
B.sut.	FPRQIAMYLSREMTD	SSLPKIGEEFGRDH	TTVIHAHEKISKLLA	D-----DEQLQ	QHVKEIKEQLK----	-----	446	
M.tub.	QSRQIAMYLCRELTD	LSLPKIGQAFG-RDH	TTVMYAQRKILSEMA	E-----RREVF	DHVKELTTRIRQRSK	R-----	507	
T.th.	LPRQLAMYLVLRELTP	ASLPEIGQLFGGRDH	TTVRYAIQKVQELAG	KP-----DREVQ	GLLRTLREACTDPVD	NLWITCG	446	
E.coli	RPRQMAMALAKELTN	HSLPEIGDAFGGRDH	TTVLHACRKIEQLRE	E-----SHDIK	EDFSNLIRTLSS----	-----	467	
T.mar.	TARRIGMYVAKNYLK	SSLRTIAEFKN-RSH	PVVVDSVKVKDSLL	KG-----NKQLK	ALIDEVIGEISRRAL	SG-----	440	
H.pyl.	LARKLVVYFARLYTP	NPTLSLAQFLDLKDH	SSISKMYSGVKMLE	EESKPFVLSLREEIK	NRLNELNDKKTAFNS	SE-----	457	

Figure 19



A)

GTGTGCGACGAGGCCGTCTGGCAACACGTTCTGGAGCACA  
 TCCGCCGCAGCATCACCGAGGTGGAGTTCCACACCTGGTT  
 TGAAAGGATCCGCCCTTGGGGATCCGGGACGGGGTGCTG 120  
 GAGCTCGCCGTGCCACCTCCTTTGCCCTGGACTGGATCC  
 GCGGCCACTACGCCGGCCTCATCCAGGAGGGCCCTCGGCT  
 CCTCGGGGCCAGGCGCCCCGGTTTGAGCTCCGGGTGGTG 240  
 CCGGGGTTCGTAGTCCAGGAGGACATCTTCCAGCCCCCGC  
 CGAGCCCCCGGCCAAGCTCAACCCGAAGATACCTTTAA  
 AACTTCGTGGTGGGGCCCAACAACCTCCATGGCCCCACGGC 360  
 GCGCCGTGGCCGTGGCCGAGTCCCCCGCGCGGCCTACA  
 ACCCCCTCTTCATCTACGGGGGCCGTGGCCTGGGAAAGAC  
 CTACCTGATGCACGCCGTGGGCCCCACTCCGTGCGAAGCGC 480  
 TTCCCCCACATGAGATTAGAGTACGTTTCCACGGAAACTT  
 TCACCAACGAGCTCATCAACCGGCCATCCGCGAGGGACCG  
 GATGACGGAGTTCCGGGAGCGGTACCGCTCCGTGGACCTC 600  
 CTGCTGGTGGACGACGTCCAGTTCATCGCCGGAAGGAGC  
 GCACCCAGGAGGAGTTTTTCCACACCTTCAACGCCCTTTA  
 CGAGGCCCACAAGCAGATCATCCTCTCCTCCGACCGGCCG 720  
 CCCAAGGACATCCTCACCTGGAGGCGCGCTGCGGAGCC  
 GCTTTGAGTGGGGCCTGATCACCGACAATCCAGCCCCCGA  
 CCTGGAACCCGGATCGCCATCCTGAAGATGAACGCCAGC 840  
 AGCGGGCCTGAGGATCCCGAGGACGCCCTGGAGTACATCG  
 CCGGCAGGTCACCTCCAACATCCGGGAGTGGGAAGGGGC  
 CCTCATGCGGGCATCGCCTTTCGCCTCCCTCAACGGCGTT 960  
 GAGCTGACCCGCGCCGTGGCGGCCAAGGCTCTCCGACATC  
 TTCGCCCCAGGGAGCTGGAGGCGGACCCCTTGGAGATCAT  
 CCGCAAAGCGGCGGGACCAAGTTCGGCCTGAAACCCCGGGA 1080  
 GGAGCTCACGGGAGCGCCGAAGAAGGAGGTGGTCTCTCC  
 CCGGCAGCTCGCCATGTACCTGGTGGCGGAGCTACCCCC  
 GGCCTCCCTGCCCGAGATCGACCAGCTCAACGACGACCGG 1200  
 GACCACACCACGGTCTCTACGCCATCCAGAAGGTCCAGG  
 AGCTCGCGGAAAGCGACCGGGAGGTGCAGGGCCTCCTCCG  
 CACCTCCGGGAGGCGTGCACATGA

B)

VSHEAVWQHVLHRRSITEVEFHTWFERIRPLGIRDGVL  
 ELAVPTSFALDWIRRHYAGLIQEGPRLPGAQAPRFELRVV  
 PGVVVQEDIFQPPSPPAQAQPEDTFKTSWWGPTTPWPHG 120  
 GAVAVAESPGRAYNPLFIYGGRLGKTYLMHAVGPLRAKR  
 FPHMRLEYVSTETFTNELINRPSARDRMTEFRERYRSVDL  
 LLVDDVQFIAGKERTQEEFFHTFNALYEAHKQIILSSDRP 240  
 PKDILTLEARLRSRFEWGLITDNPAPDLETRIAILKMNAS  
 SGPEDPEDALEYIARQVTSNIREWEGALMRASPFASLNGV  
 ELTRAVALKALRHLRPRELEADPLEIRKAAGPVRPETPG 360  
 GAHGERRKKEVVLPRQLAMYLVRELTPASLPEIDQLNDDR  
 DHTTVLYAIQKVQELAESDREVQGLLRTLREACT

Figure 20

A)

ATGAACATAACGGTTCCCAAAAACTCCTCTCGGACCAGC 40  
 TTTCCCTCCTGGAGCGCATCGTCCCCTCTAGAAGCGCCAA  
 CCCCCTCTACACCTACCTGGGGCTTTACGCCGAGGAAGGG 120  
 GCCTTGATCCTCTTCGGGACCAACGGGGAGGTGGACCTCG  
 AGGTCCGCCTCCCCGCCGAGGCCCAAAGCCTTCCCCGGGT 200  
 GCTCGTCCCCCGCCCAGCCCTTCTTCCAGCTGGTGGGAGC  
 CTTCTGGGGACCTCGTGGCCCTCGGCCTCGCCTCGGAGC 280  
 CGGGCCAGGGGGGGCAGCTGGAGCTCTCCTCCGGGCGTTT  
 CCGCACCCGGCTCAGCCTGGCCCTGCCGAGGGCTACCCC 360  
 GAGCTTCTGGTGGCCGAGGGGGAGGACAAGGGGGCCTTCC  
 CCCTCCGGACGCGGATGCCCTCCGGGGAGCTCGTCAAGGC 440  
 CTTGACCCACGTGCGCTACGCCGCGAGCAACGAGGAGTAC  
 CGGGCCATCTTCCGCGGGGTGCAGCTGGAGTTCTCCCCC 520  
 AGGGCTTCCGGGCGGTGGCCTCCGACGGGTACCGCCTCGC  
 CCTCTACGACCTGCCCCCTGCCCAAGGGTTCCAGGCCAAG 600  
 GCCGTGGTCCCCGCCCGGAGCGTGGACGAGATGGTGGGG  
 TCCTGAAGGGGGCGGACGGGGCCGAGGCCGTCTCGCCCT 680  
 GGGCGAGGGGGTGTGGCCCTGGCCCTCGAGGGCGGAAGC  
 GGGGTCCGGATGGCCCTCCGCCTCATGGAAGGGGAGTTCC 760  
 CCGACTACCAGAGGGTCATCCCCCAGGAGTTGCCCTCAA  
 GGTCCAGGTGGAGGGGGAGGCCCTCAGGGAGGCGGTGCGC 840  
 CGGGTGAGCGTCCTCTCCGACCGGCAGAACACCGGGTGG  
 ACCTCCTTTTGGAGGAAGGCCGGATCCTCCTCTCCGCCGA 920  
 GGGGGACTACGGCAAGGGGCAGGAGGAGGTGCCCGCCCAG  
 GTGGAGGGGCCGGACATGGCCGTGGCCTACAACGCCCGCT 1000  
 ACCTCCTCGAGGCCCTCGCCCCGTGGGGGACCGGGCCCA  
 CCTGGGCATCTCCGGGCCCCACGAGCCCGAGCCTCATCTGG 1080  
 GGGGACGGGGAGGGGTACCGGGCGGTGGTGGTGGCCCTCA  
 GGGTCTAG 1128

B)

MNITVPPKLLSDQLSLLERIVPSRSANPLYTYLGLYAEAG 40  
 ALILFGTNGEVDLEVRPAEAQSLPRVLVPAQPFQLVRS  
 LPGDLVALGLASEPGGQLELSSGRFRTRLSLAPAEGY 120  
 ELLVPEGEDKGAFLRTRMPSELVKALTHVRYAASNEEY  
 RAIFRGVQLEFSPQGFRAVASDGYRLALYDLPLPQGFQAK 200  
 AVVPARSVDEMVRVLKGADGAEAVLALGEGVLALALEGGS  
 GVRMALRLMEGEFPDYQRVIPQEFALKVQVEGEALREAVR 280  
 RVSVLSDRQNHRVDLLLEGRILLSAEGDYKGQEEVPAQ  
 VEGPDMAYAYNARYLLEALAPVGDRHLGISGPTSPSLIW 360  
 GDGEGYRAVVVPLRVZ

Figure 21

[illegible]

Figure 22

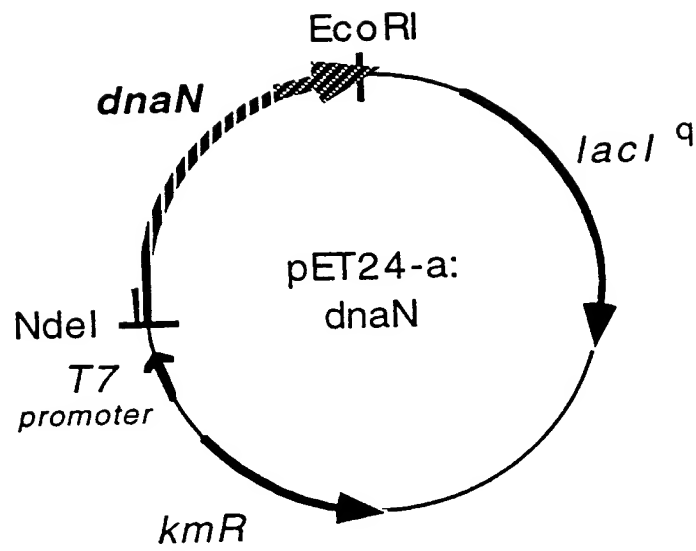
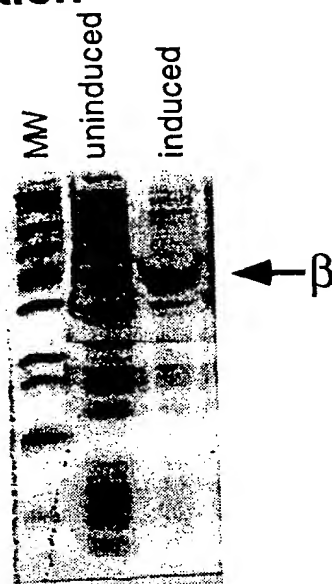


Figure 23

**A) Induction**

↓  
**Lysis**  
↓  
**Heat Step**  
↓

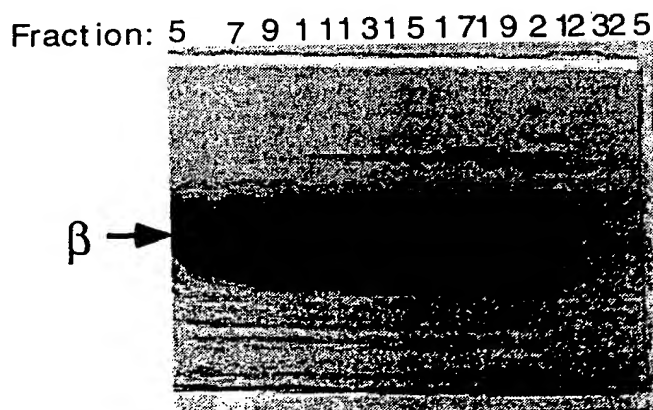
**B) MonoQ Column**

Figure 24

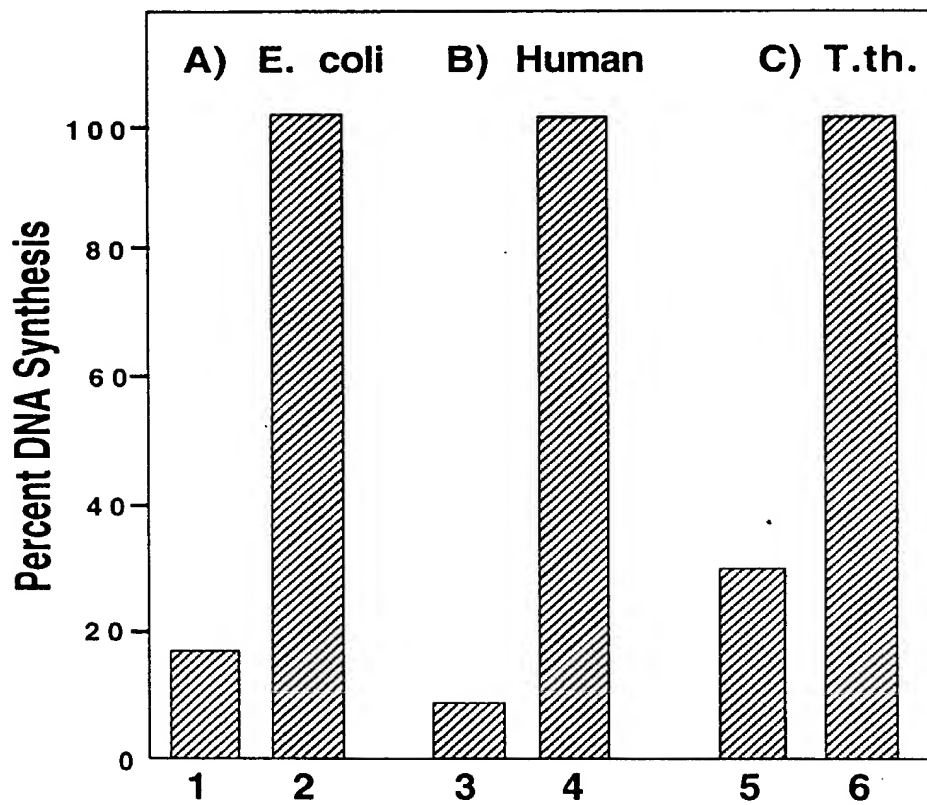
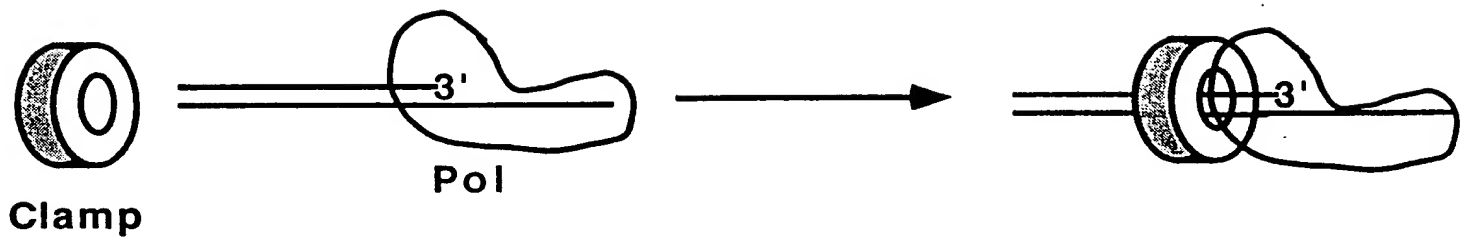


Figure 25

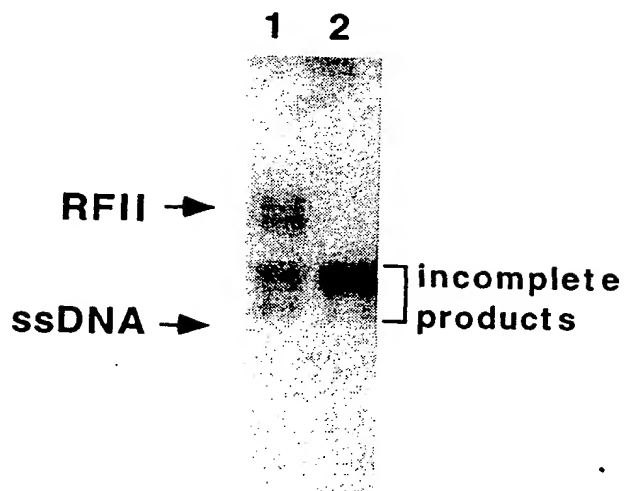
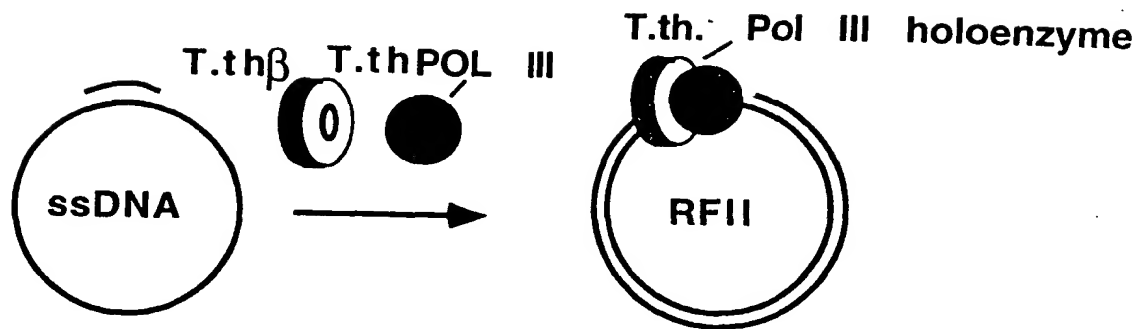


Figure 26